Information-theoretic analysis of high-order interactions in physiological networks of oscillatory processes

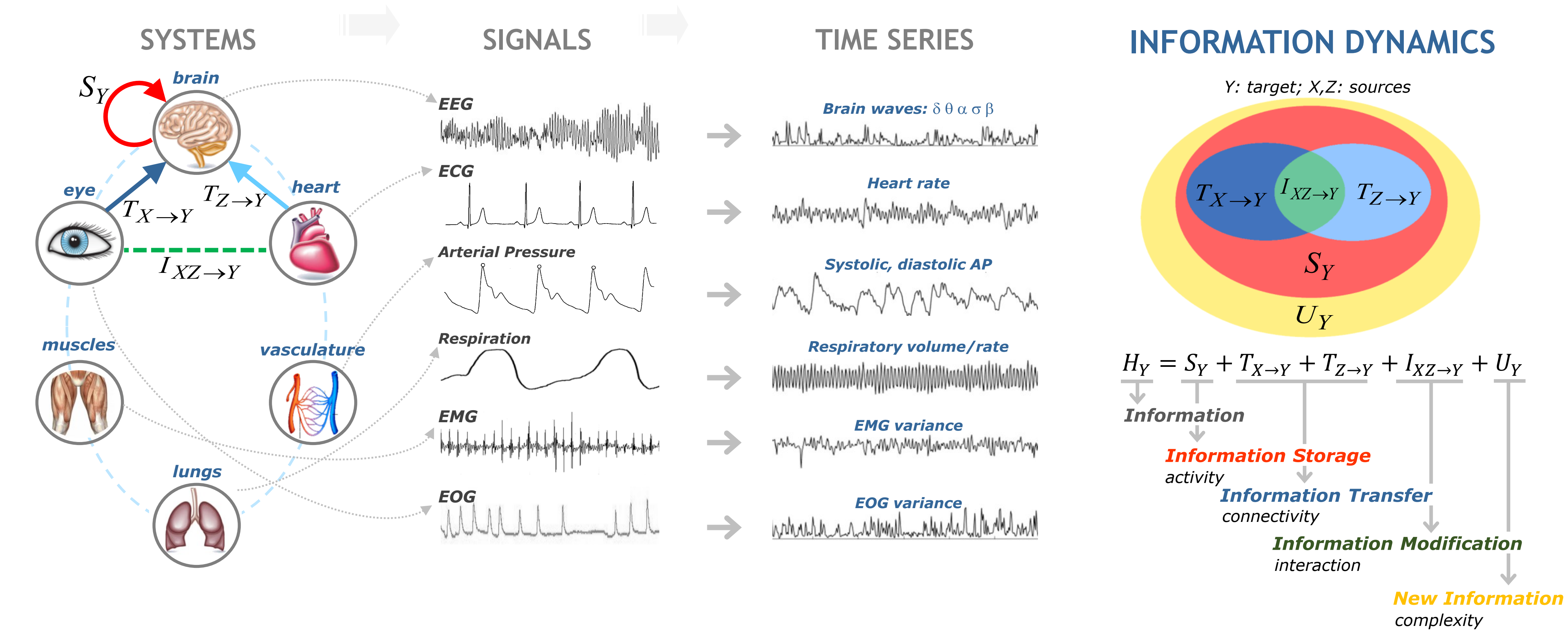
Luca Faes

Department of Engineering

University of Palermo, Italy

Exploring Network Physiology with Information Theory

- Framework of Information Dynamics to assess physiological interactions



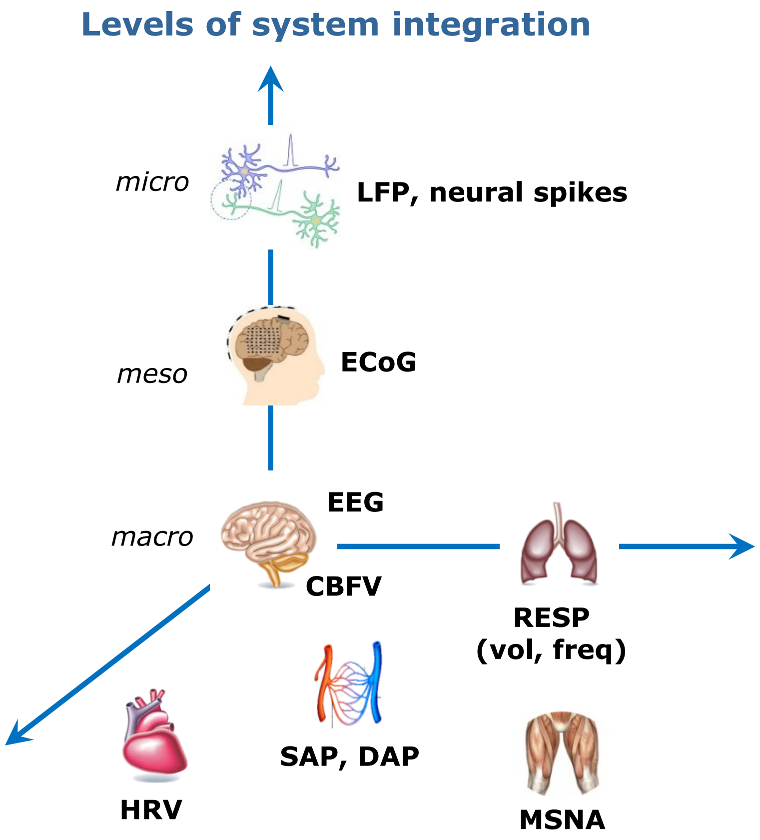
Theoretical design and implementation of the framework of Information Dynamics:

L Faes, A Porta, G Nollo, M Javorka, 'Information decomposition in multivariate systems: definitions, implementation and application to cardiovascular networks', *Entropy* 2017, 19(1), 5

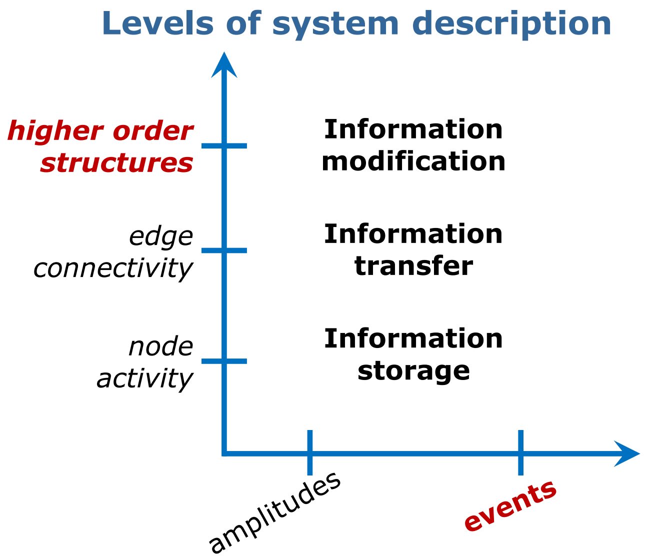
L Faes, G Nollo, A Porta: 'Information decomposition: a tool to break down cardiovascular and cardiorespiratory complexity', Complexity and Nonlinearity in Cardiovascular Signals, *Springer*; 2017, pp.87-113

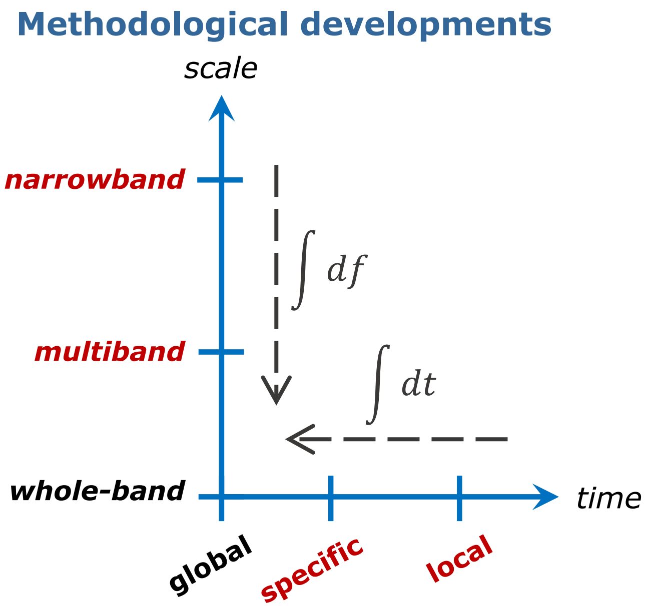
The framework of Information Dynamics: Developments

- The measures of information dynamics are defined for discrete-time processes, and have been developed mostly in the time domain



- Extensions of the framework of Information Dynamics:

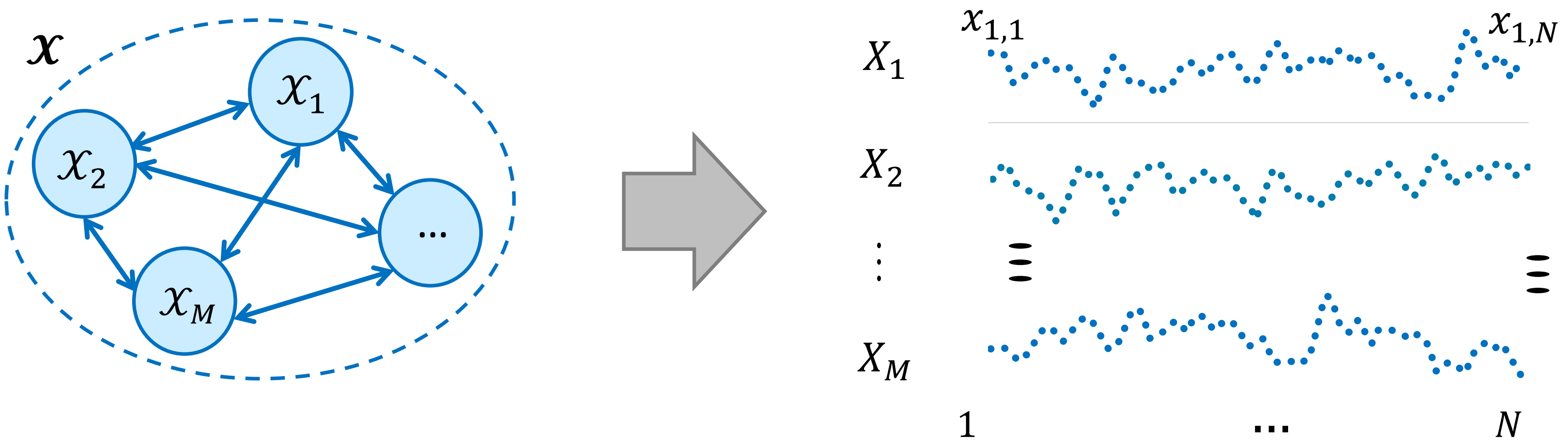




- ***Aim***: to generalize the framework of information dynamics to assess pairwise and higher-order physiological interactions in the time and frequency domains

Information-theoretic description of physiological time series: **STATIC ANALYSIS**

- Static analysis: Dynamic System $\boldsymbol{\mathcal{X}} = \{\mathcal{X}_1, \mathcal{X}_2, \ldots, \mathcal{X}_M\}$ Vector of random variables $\boldsymbol{X} = [X_1 X_2 \cdots X_M]$



- Assumption: *i.i.d. random variables* (temporal independence) → STATIC analysis
  temporal correlations disregarded; interactions computed at lag 0

- Assumption: ***stationarity***: the i.i.d. variables are studied from a single multivariate time series $\mathbf{X}$

- Realization of $\boldsymbol{X}$: M time series of length N, collected in the data matrix $\mathbf{X} = \begin{bmatrix} x_{1,1} & \cdots & x_{M,1} \\ \vdots & \ddots & \vdots \\ x_{1,N} & \cdots & x_{M,N} \end{bmatrix}$

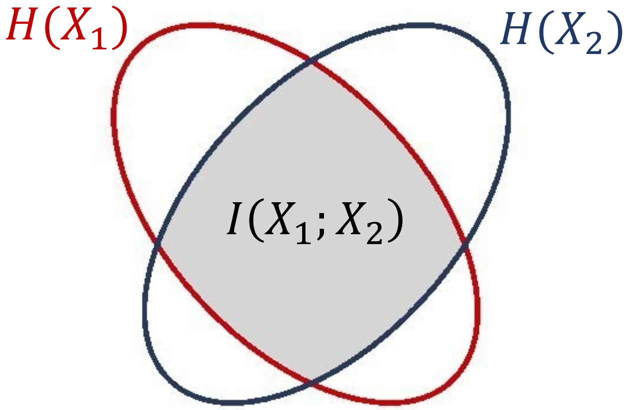
Information-theoretic analysis of static interactions

- Information content: ENTROPY

$$H(X_1) = \mathbb{E}\left[\log \frac{1}{p(x_1)}\right]$$

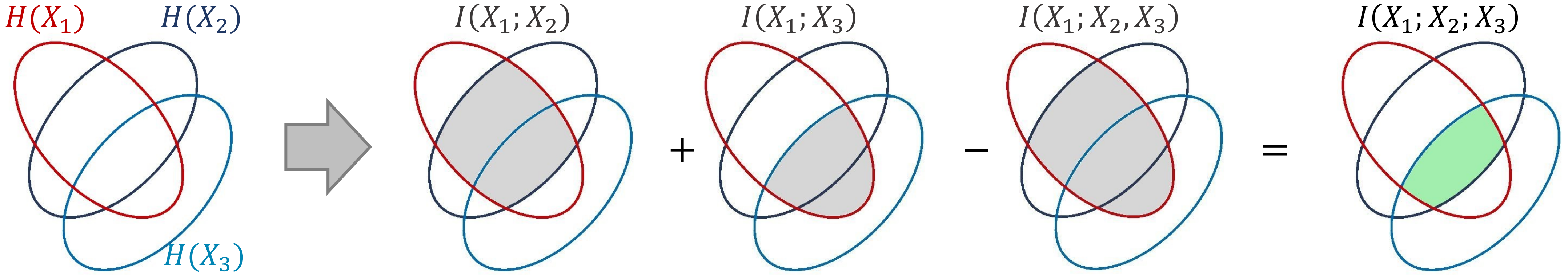
- Interactions of order 2: MUTUAL INFORMATION

$$I(X_1;X_2) = \mathbb{E}\left[log \frac{p(x_1,x_2)}{p(x_1)p(x_2)}\right] = H(X_1) + H(X_2) - H(X_1,X_2)$$



- Interactions of order 3: INTERACTION INFORMATION $I(X_1;X_2;X_3) = I(X_1;X_2) + I(X_1;X_3) - I(X_1;X_2,X_3)$

[W McGill, Psychometrika 19, 1954]



$I(X_1;X_2,X_3) < I(X_1;X_2) + I(X_1;X_3)$

$I(X_1;X_2;X_3) > 0$: ***redundancy***

$I(X_1;X_2,X_3) > I(X_1;X_2) + I(X_1;X_3)$

$I(X_1;X_2;X_3) < 0$: ***synergy***

Information-theoretic analysis of HIGHER-ORDER interactions

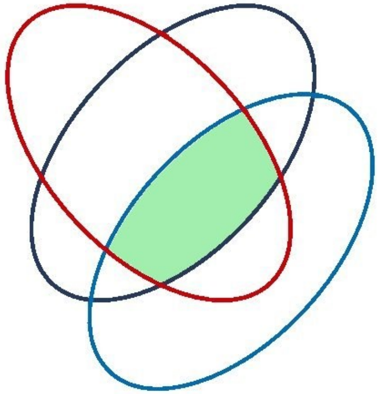
- Interactions of order ≥3: O-INFORMATION
[FE Rosas et al, Phys Rev E 100, 2019]

$$X^N = \{X_1, \dots, X_N\}$$

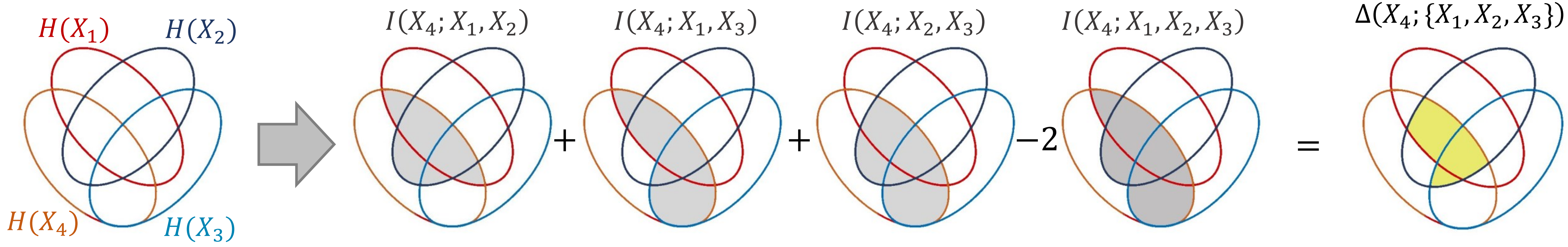
$$\Omega(X^N) = \Omega(X^N_{-j}) + \Delta(X_j; X^N_{-j})$$

$$\Delta(X_j; X^N_{-j}) = \sum_{\substack{m=1 \\ m\neq j}}^{N} I(X_j; X^N_{-mj}) + (2-N) I(X_j; X^N_{-j})$$

- $N = 3 : \Omega(X^3) = I(X_1; X_2; X_3)$



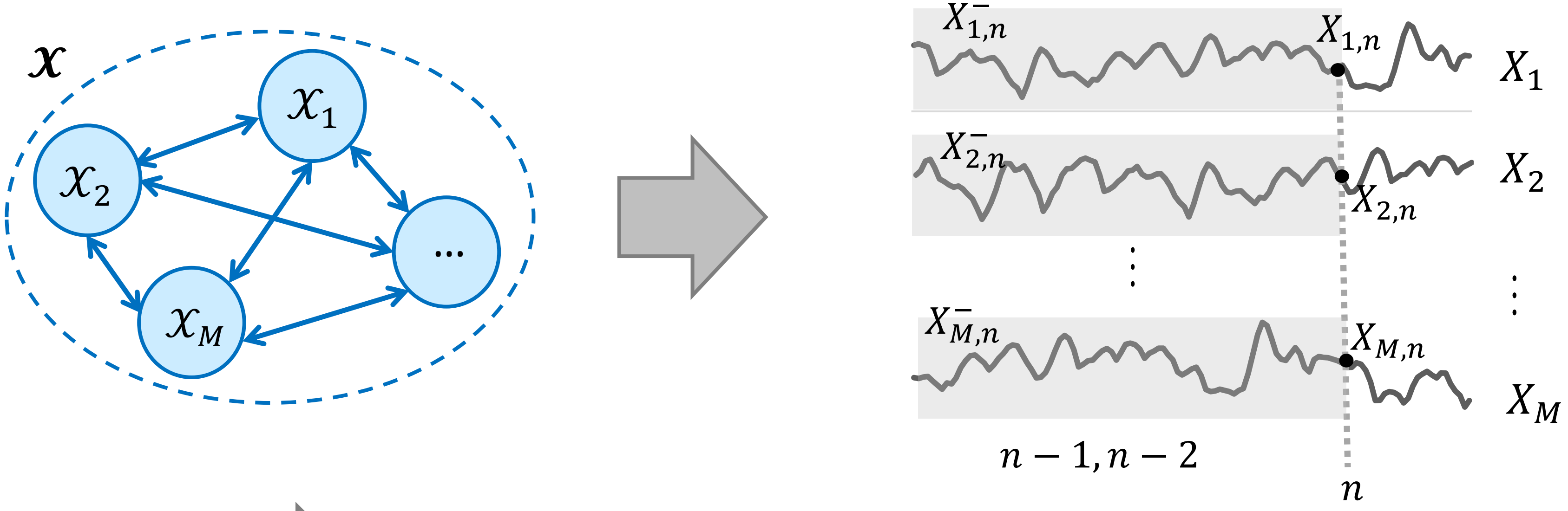
- $N = 4 : \Delta(X_4; \{X_1, X_2, X_3\}) = I(X_4; X_1, X_2) + I(X_4; X_1, X_3) + I(X_4; X_2, X_3) - 2I(X_4; X_1, X_2, X_3)$



- The sign of $\Delta(X_j; X^N_{-j})$ and $\Omega(X^N)$ reflects the redundant (+) or synergistic (-) nature of the interactions in X^N

Information-theoretic description of physiological time series: **DYNAMIC ANALYSIS**

- Limitation of static analysis of random variables: the temporal information is disregarded
- Dynamic analysis: Dynamic System $\boldsymbol{\mathcal{X}} = \{\mathcal{X}_1, \mathcal{X}_2, \dots, \mathcal{X}_M\}$ Vector of random processes $\boldsymbol{X} = [X_1 X_2 \cdots X_M]$

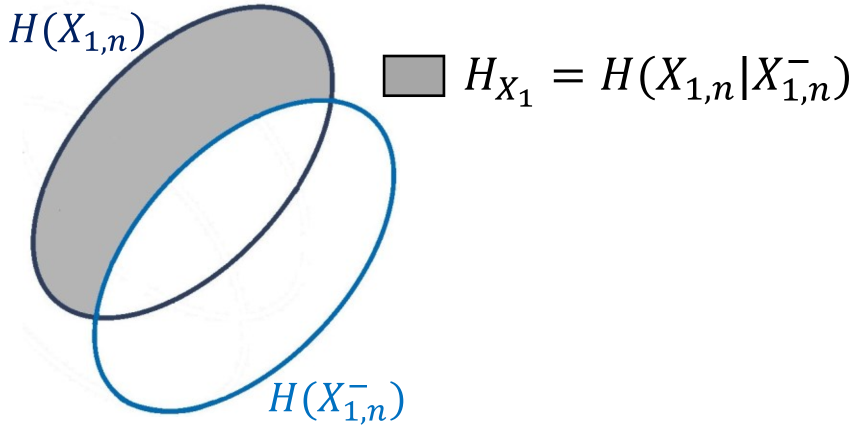


- Assumption: ***i.d. random variables*** → Dynamic analysis
- temporal correlations are explicitly considered → study of dependencies between $X_{i,n}$ and $X_{j,n}^-$
- Assumption: ***stationarity***: the i.d. variables are studied from a single multivariate time series $\mathbf{X}$
- Realization of $\boldsymbol{X}$: M time series of length N, collected in the data matrix $\mathbf{X} = \begin{bmatrix} x_{1,1} & \cdots & x_{M,1} \\ \vdots & \ddots & \vdots \\ x_{1,N} & \cdots & x_{M,N} \end{bmatrix}$

Information-theoretic analysis of dynamic interactions: PAIRWISE ANALYIS

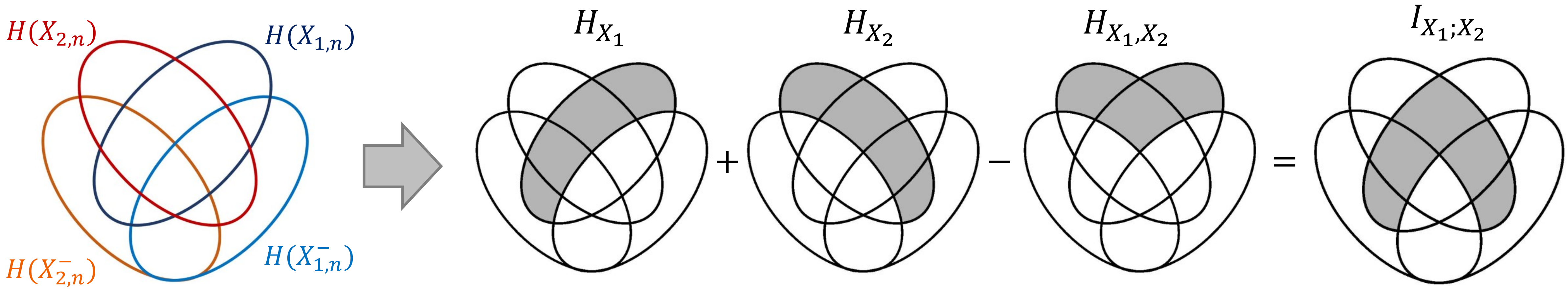
- Information content: ENTROPY RATE

$$H_{X_1} \triangleq \lim_{N\to\infty} \frac{1}{N} H\left(X_{1,n:n+N}\right) = H(X_{1,n}|X_{1,n}^-)$$ ⇨ *Complexity measure*



- Interactions of order 2: MUTUAL INFORMATION RATE (MIR)

$$I_{X_1;X_2} \triangleq \lim_{N\to\infty} \frac{1}{N} I\left(X_{1,n:n+N};X_{2,n:n+N}\right) = H_{X_1} + H_{X_2} - H_{X_1,X_2}$$ ⇨ *Measure of dynamic coupling*



Assessment of Higher-Order interactions in random processes

- Interactions of order ≥3:

  O-INFORMATION RATE (OIR)

  $$X^N = \{X_1, \dots, X_N\}$$

  $$\Omega_{X^N} = \Omega_{X^N_{-j}} + \Delta_{X_j;X^N_{-j}}$$

  $$\Delta_{X_j;X^N_{-j}} = \sum_{\substack{m=1 \\ m\neq j}}^{N} I_{X_j;X^N_{-mj}} + (2-N) I_{X_j;X^N_{-j}}$$

- Recursive definition:
  - $N = 2$: $\Omega_{X^2} = 0$
  - $N = 3$: *Interaction information rate*

    $$\Omega_{X^3} = \Delta_{X_3;\{X_1,X_2\}} = I_{X_3;X_1} + I_{X_3;X_2} - I_{X_3;\{X_1,X_2\}}$$
  - $N = 4$: *O-information rate*

    $$\Omega_{X^4} = \Omega_{X^3} + \Delta_{X_4;\{X_1,X_2,X_3\}}$$

    $$\Delta_{X_4;\{X_1,X_2,X_3\}} = I_{X_4;X_1,X_2} + I_{X_4;X_1,X_3} + I_{X_4;X_2,X_3} - 2I_{X_4;X_1,X_2,X_3}$$

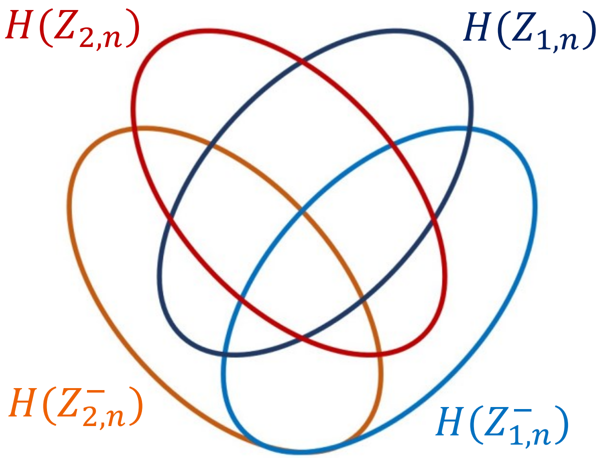
- The sign of Ω_{X^N} and $\Delta_{X_j;X^N_{-j}}$ reflects the redundant (+) or synergistic (-) nature of the interactions in X^N

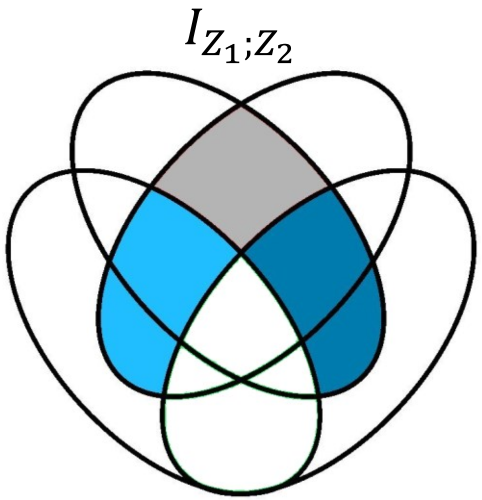
- *COMPUTATION*:
  - All measures of dynamic information quantifying high-order interactions can be computed as the sum of MIR terms involving two or more processes X_i
  - Computation amounts to quantify $I_{Z_1;Z_2}$, with $Z_1 = X_j, Z_2 = X^N_{-mj}, j \in \{1, \dots, N\}, m \in \{0,1,\dots,N\}$

L Faes, G Mijatovic, Y Antonacci, R Pernice, C Barà, L Sparacino, M Sammartino, A Porta, D Marinazzo, S Stramaglia, 'A new framework for the time- and frequency-domain assessment of high-order interactions in brain and physiological networks', **arXiv:2202.04179, 2022**

- Expansion of the Mutual Information rate
  [D Chicharro, Biol Cyb 105, 2011]

$$I_{Z_1;Z_2} = I\left(Z_{1,n}; Z_{2,n}^{-} | Z_{1,n}^{-}\right) + I\left(Z_{2,n}; Z_{1,n}^{-} | Z_{2,n}^{-}\right) + I\left(Z_{1,n}; Z_{2,n} | Z_{1,n}^{-}, Z_{2,n}^{-}\right)$$





Transfer Entropies:
[T Schreiber, Phys Rev Lett 85, 2000]

$I\left(Z_{1,n}; Z_{2,n}^{-} | Z_{1,n}^{-}\right) = T_{Z_2 \to Z_1}$

$I\left(Z_{2,n}; Z_{1,n}^{-} | Z_{2,n}^{-}\right) = T_{Z_1 \to Z_2}$

Information shared at lag zero:

$I\left(Z_{1,n}; Z_{2,n} | Z_{1,n}^{-}, Z_{2,n}^{-}\right) = I_{Z_1 \cdot Z_1}$

- Information-theoretic decomposition of the Mutual information Rate:

$$I_{Z_1;Z_2} = T_{Z_1 \to Z_2} + T_{Z_2 \to Z_1} + I_{Z_1 \cdot Z_2}$$

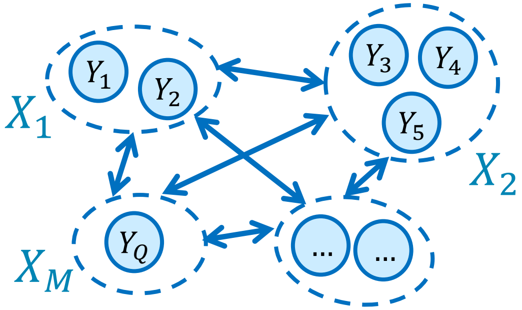
coupling ($I_{Z_1;Z_2}$) — causal interaction ($T_{Z_1 \to Z_2} + T_{Z_2 \to Z_1}$) — instantaneous causality ($I_{Z_1 \cdot Z_2}$)

- Dynamic Information Exchange (MIR): $I_{Z_1;Z_2}$
- Information transfer (Transfer Entropy, TE): $T_{Z_1 \to Z_2}, T_{Z_2 \to Z_1}$
- Instantaneous information sharing: $I_{Z_1 \cdot Z_2}$

Computation of MIR and OIR based on linear Vector Autoregressive Models

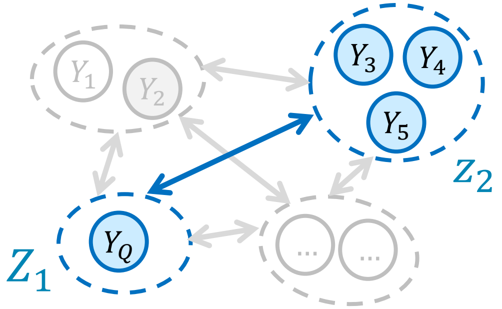
- Q random processes $Y = \{Y_1, \dots, Y_Q\}$ collected in M blocks $X_1, \dots, X_M$

- Vector autoregressive (VAR) representation of Y: $Y_n = \sum_{k=1}^{p} A_k Y_{n-k} + U_n$



- Reduced VAR models for $Z = \{Z_1, Z_2\}$ collecting some of the X processes:

$$Z_{1,n} = \sum_{k=1}^{\infty} C_{1,k} Z_{1,n-k} + V_{1,n} \qquad Z_{2,n} = \sum_{k=1}^{\infty} C_{2,k} Z_{1,n-k} + V_{2,n} \qquad Z_n = \sum_{k=1}^{\infty} B_k Z_{n-k} + W_n$$



- Estimation of the innovation covariance matrices through the theory of state space models: $\mathbf{\Sigma}_W = \mathbb{E}[WW^{\mathrm{T}}], \mathbf{\Sigma}_{V_1} = \mathbb{E}\left[V_1 V_1^{\mathrm{T}}\right], \mathbf{\Sigma}_{V_2} = \mathbb{E}[V_2 V_2^{\mathrm{T}}]$
  [L Barnett et al, Phys Rev E 91, 2015]

- Computation of TE, instantaneous information and MIR exploiting the analogy between TE and Granger causality valid for Gaussian processes: [L Barnett et al, Phys Rev Lett 103, 2009]

$$T_{Z_1 \to Z_2} = \frac{1}{2} \log \frac{|\mathbf{\Sigma}_{V_2}|}{|\mathbf{\Sigma}_{W_{22}}|}, T_{Z_2 \to Z_1} = \frac{1}{2} \log \frac{|\mathbf{\Sigma}_{V_1}|}{|\mathbf{\Sigma}_{W_{11}}|} \qquad I_{Z_1 \cdot Z_2} = \frac{1}{2} \log \frac{|\mathbf{\Sigma}_{W_{11}}||\mathbf{\Sigma}_{W_{22}}|}{|\mathbf{\Sigma}_W|} \qquad I_{Z_1 ; Z_2} = \frac{1}{2} \log \frac{|\mathbf{\Sigma}_{V_1}||\mathbf{\Sigma}_{V_2}|}{|\mathbf{\Sigma}_W|}$$

Frequency-domain expansion of MIR

- Discrete-time Fourier transform of Z_n : $Z(\omega) = \left[\mathbf{I} - \sum_{k=1}^{\infty} B_k\, e^{-j\omega k}\right]^{-1} W(\omega) = \mathbf{H}(\omega)W(\omega)$

- Power spectral density of Z_n : $\mathbf{S}_Z(\omega) = \mathbf{H}(\omega)\boldsymbol{\Sigma}_W\mathbf{H}^*(\omega) = \begin{bmatrix} \mathbf{S}_{Z_1}(\omega) & \mathbf{S}_{Z_1Z_2}(\omega) \\ \mathbf{S}_{Z_2Z_1}(\omega) & \mathbf{S}_{Z_1}(\omega) \end{bmatrix}$

- Frequency-domain measures of TE, Instantaneous information and MIR :

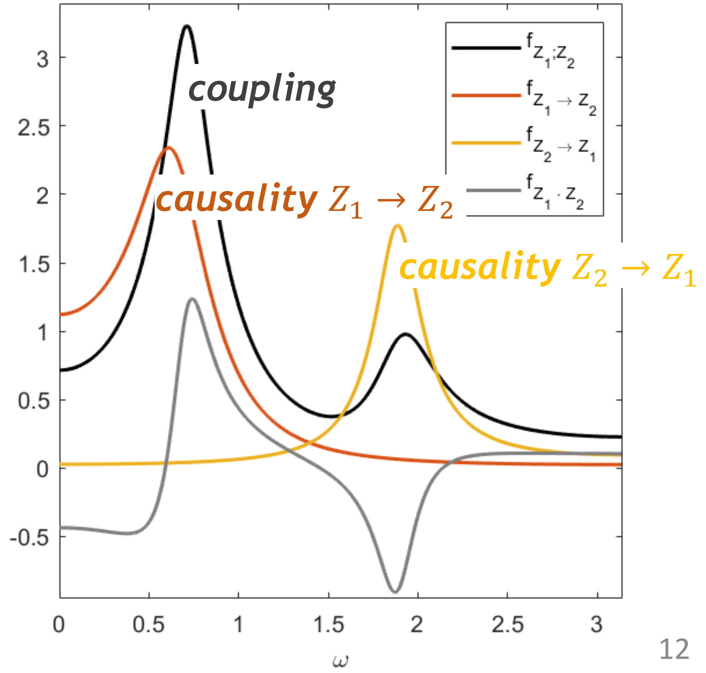
$$f_{Z_1\to Z_2}(\omega) = \log\frac{|\mathbf{S}_{Z_2}(\omega)|}{|\mathbf{H}_{22}(\omega)\boldsymbol{\Sigma}_{W_{22}}\mathbf{H}^*_{22}(\omega)|} \qquad f_{Z_2\to Z_1}(\omega) = \log\frac{|\mathbf{S}_{Z_1}(\omega)|}{|\mathbf{H}_{11}(\omega)\boldsymbol{\Sigma}_{W_{11}}\mathbf{H}^*_{11}(\omega)|}$$

$$f_{Z_1\cdot Z_2}(\omega) = \log\frac{|\mathbf{H}_{11}(\omega)\boldsymbol{\Sigma}_{W_{11}}\mathbf{H}^*_{11}(\omega)||\mathbf{H}_{22}(\omega)\boldsymbol{\Sigma}_{W_{22}}\mathbf{H}^*_{22}(\omega)|}{|\mathbf{S}_Z(\omega)|}$$

[J Geweke, J Am Stat Ass 77, 1982]

$$f_{Z_1;Z_2}(\omega) = f_{Z_1\to Z_2}(\omega) + f_{Z_2\to Z_1}(\omega) + f_{Z_1\cdot Z_2}(\omega)$$

[D Chicharro, Biol Cyb 105, 2011]



- Integration of the spectral information measures yields the time domain information measures:

$$I_{Z_1;Z_2} = \frac{1}{4\pi}\int_{-\pi}^{\pi} f_{Z_1;Z_2}(\omega)\,d\omega \qquad I_{Z_1\to Z_2} = \frac{1}{4\pi}\int_{-\pi}^{\pi} f_{Z_1\to Z_2}(\omega)\,d\omega$$

Time- and frequency-domain OIR based on VAR models

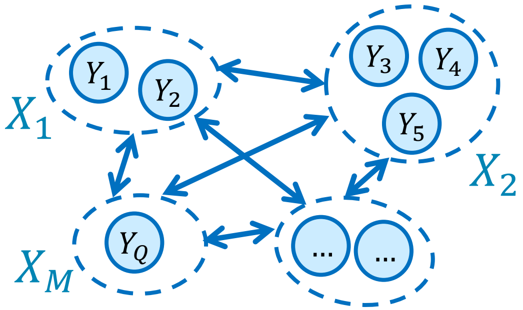
Time-domain:

Frequency-domain:

- *OIR gradient:* $\Delta_{X_j;X_{-j}^N} = \sum_{\substack{m=1 \\ m\neq j}}^{N} I_{X_j;X_{-mj}^N} + (2-N) I_{X_j;X_{-j}^N}$ ⟺ $\delta_{X_j;X_{-j}^N}(\omega) = \sum_{\substack{m=1 \\ m\neq j}}^{N} f_{X_j;X_{-mj}^N}(\omega) + (2-N) f_{X_j;X_{-j}^N(\omega)}$

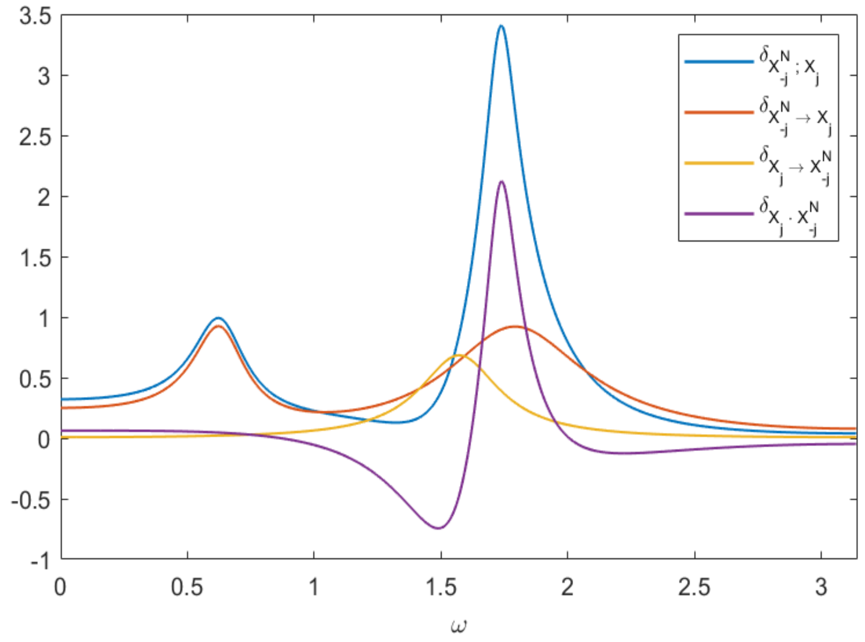
- *OIR :* $\Omega_{X^N} = \Omega_{X_{-j}^N} + \Delta_{X_j;X_{-j}^N}$ ⟺ $\nu_{X^N}(\omega) = \nu_{X_{-j}^N}(\omega) + \delta_{X_j;X_{-j}^N}(\omega)$

- Framework for the evaluation of both pairwise and higher-order dynamic interactions, in time and frequency domains



- Full-frequency integration of the spectral OIR yields the time-domain OIR:

$$\Delta_{X_j;X_{-j}^N} = \frac{1}{4\pi}\int_{-\pi}^{\pi} \delta_{X_j;X_{-j}^N}(\omega)\, d\omega \qquad \Omega_{X^N} = \frac{1}{4\pi}\int_{-\pi}^{\pi} \nu_{X^N}(\omega)\, d\omega$$



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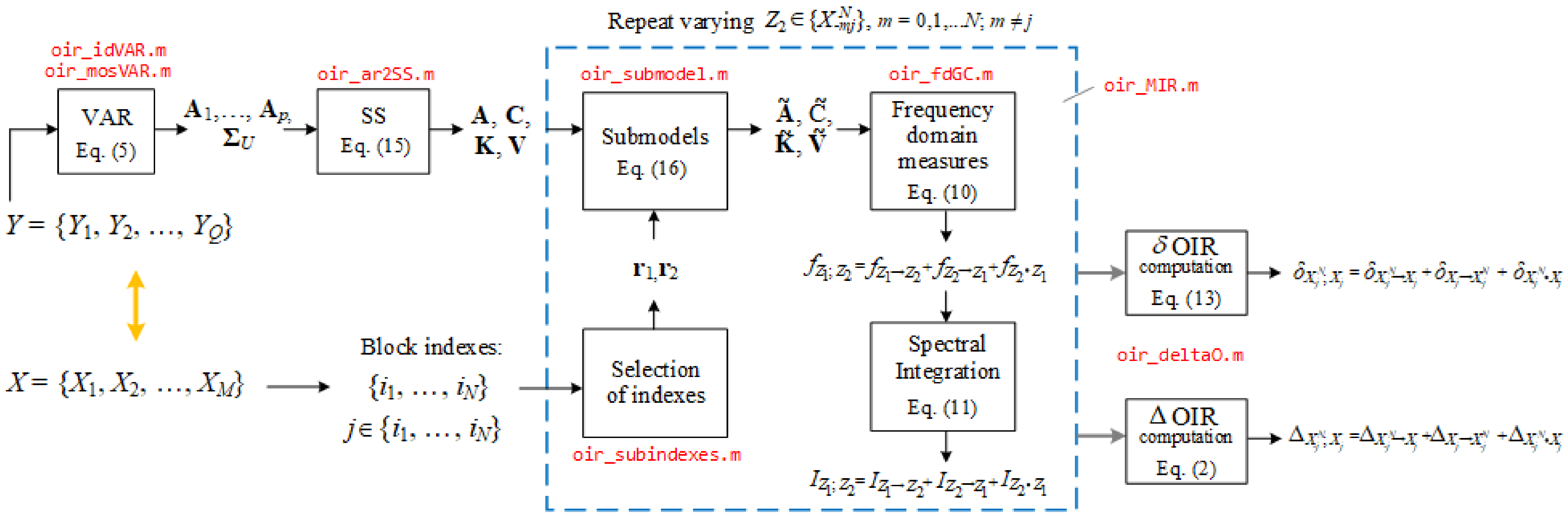
OIR Matlab toolbox

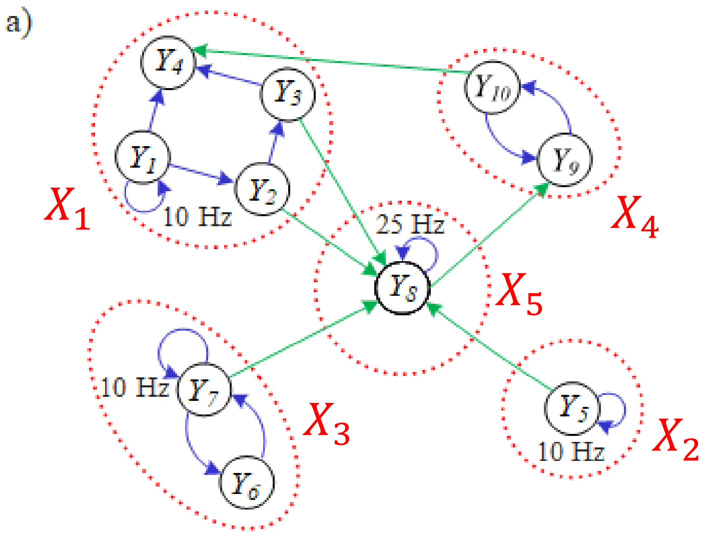
- Toolbox for the computation of time-domain and frequency-domain pairwise and higher-order interactions in networks of multiple stochastic processes



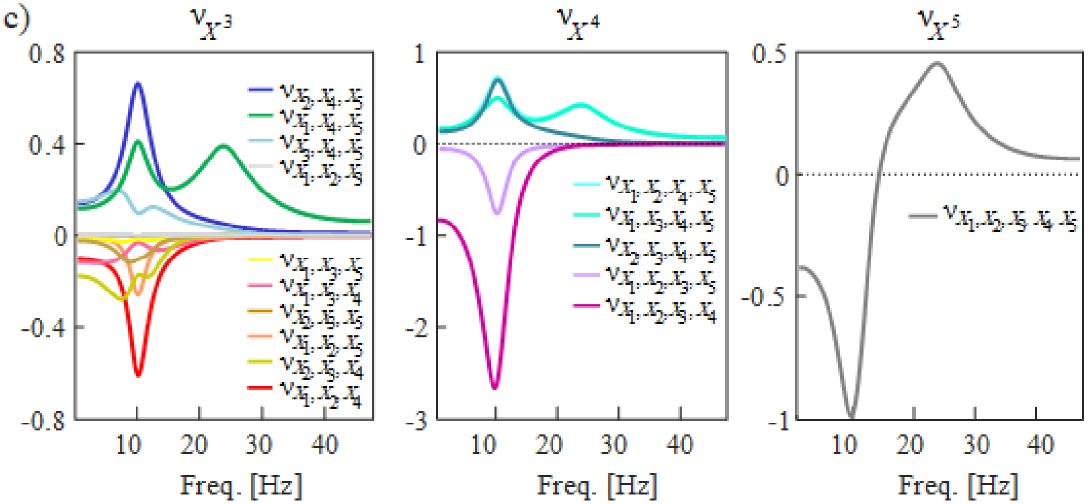
http://www.lucafaes.net/OIR.html

L Faes, G Mijatovic, Y Antonacci, R Pernice, C Barà, L Sparacino, M Sammartino, A Porta, D Marinazzo, S Stramaglia, 'A new framework for the time- and frequency-domain assessment of high-order interactions in brain and physiological networks', **arXiv:2202.04179, 2022**

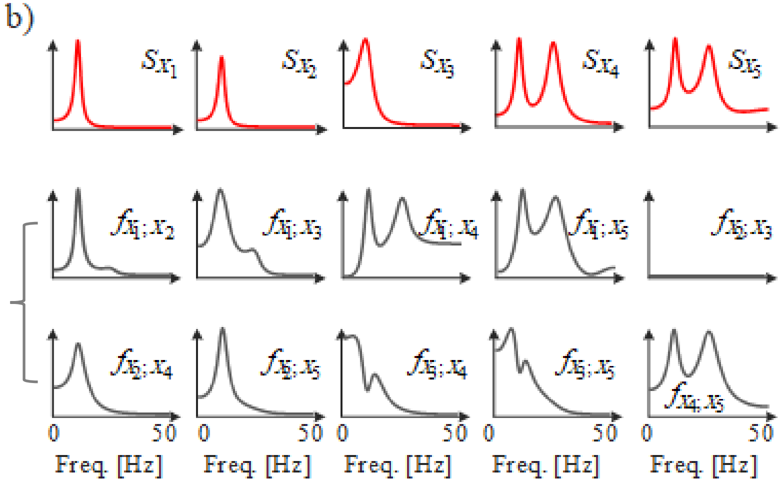
- Simulation of $Q = 10$ random processes grouped in $M = 5$ blocks

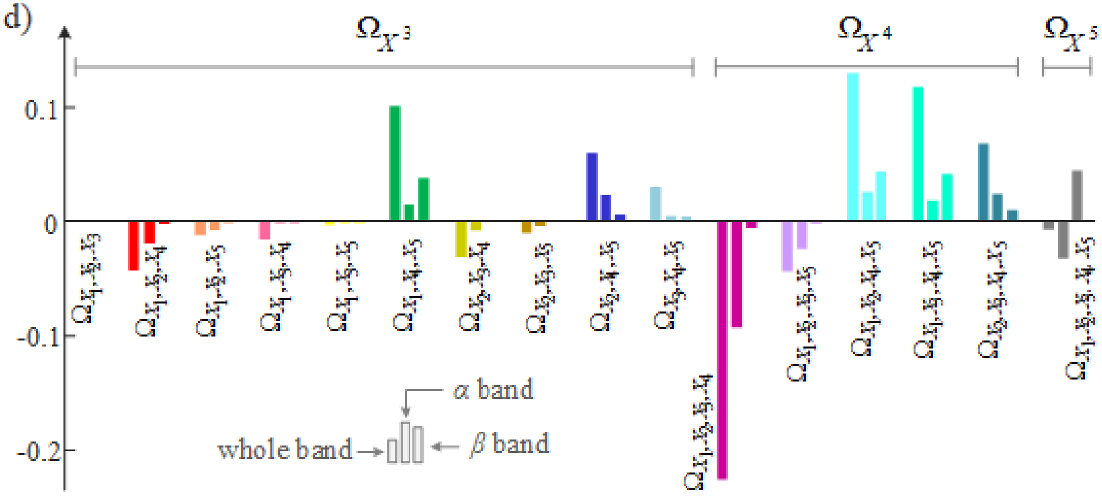


- $N = 3$: IIR
- $N = 4$: OIR
- $N = 5$: OIR



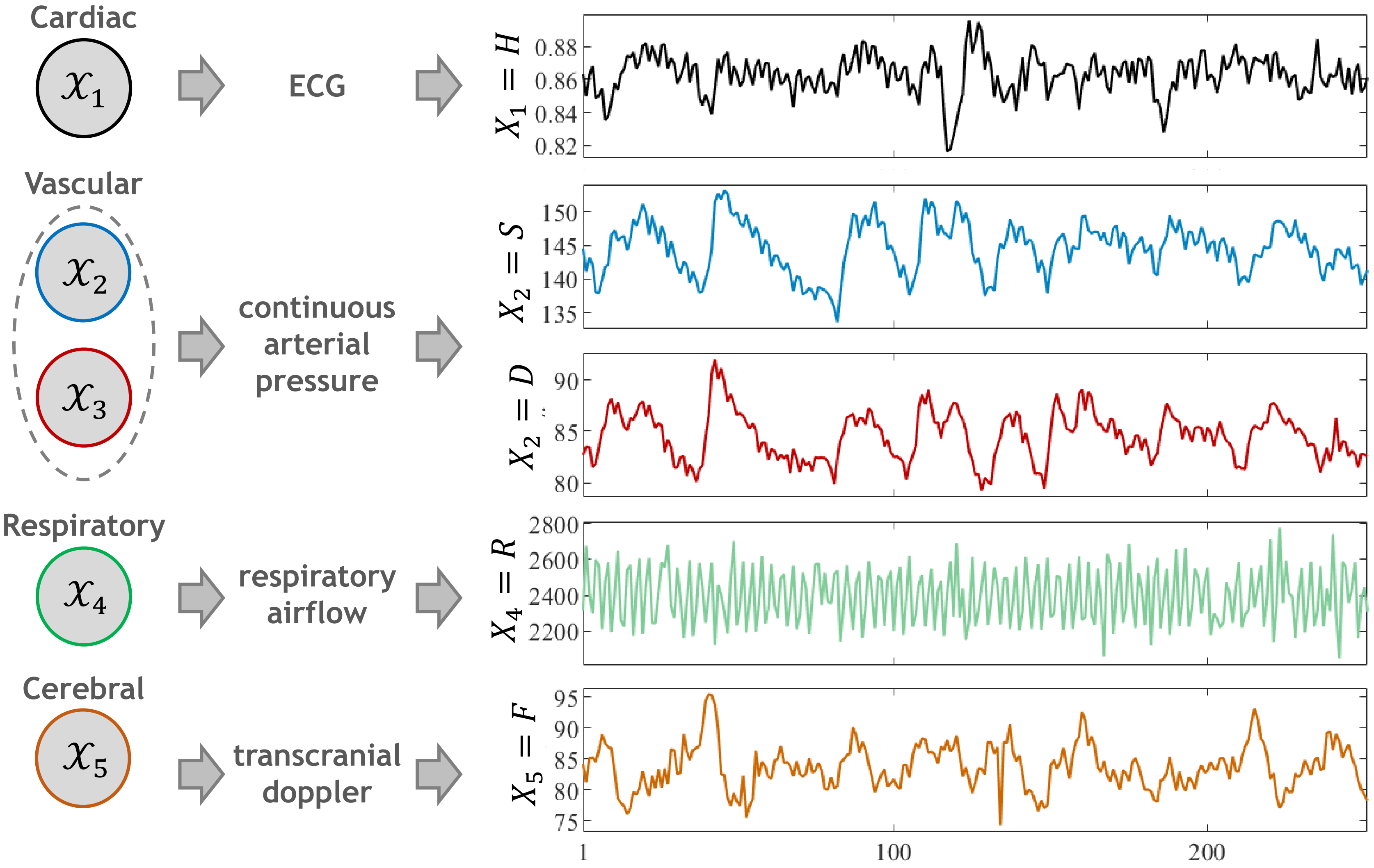
- $N = 1$: PSD
- $N = 2$: MIR





Application: cardiovascular, cerebrovascular and respiratory interactions

Systems *Signals* *Processes and time series:*



Experimental protocols

- 18 healthy subjects, resting supine position
  - Spontaneous breathing (SB)

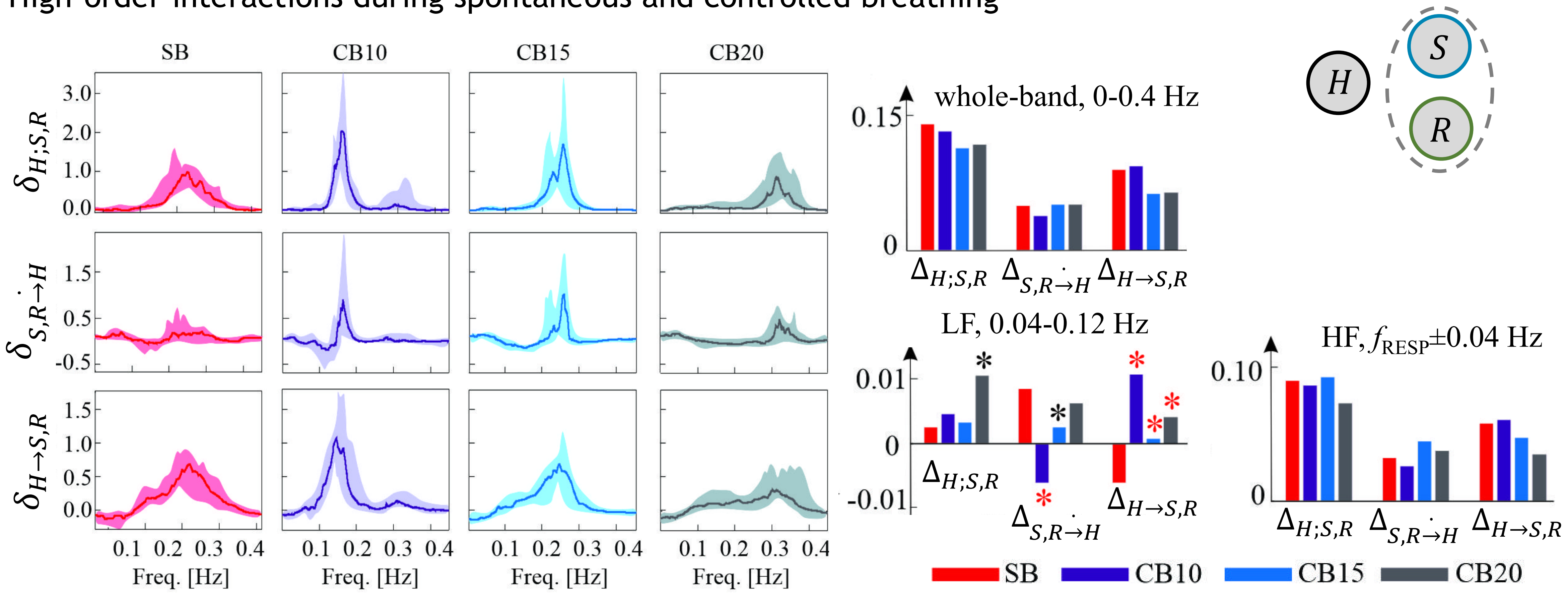
  Controlled breathing:
  - 10 breaths/min (CB10)
  - 15 breaths/min (CB15)
  - 20 breaths/min (CB20)
- 13 healthy subjects, spontaneous breathing
  - Supine position (REST)
  - Upright position (TILT)

Data Analysis

- Stationary series, *N*=250
- VAR model fitting
- OIR (time, spectral)

Application: cardiovascular and respiratory interactions

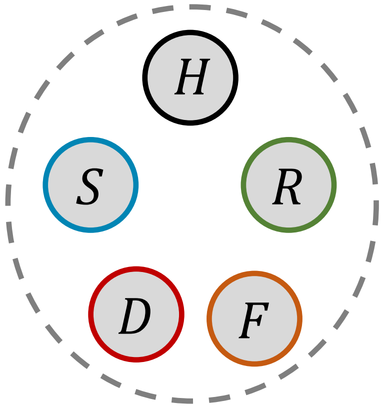
- High-order interactions during spontaneous and controlled breathing

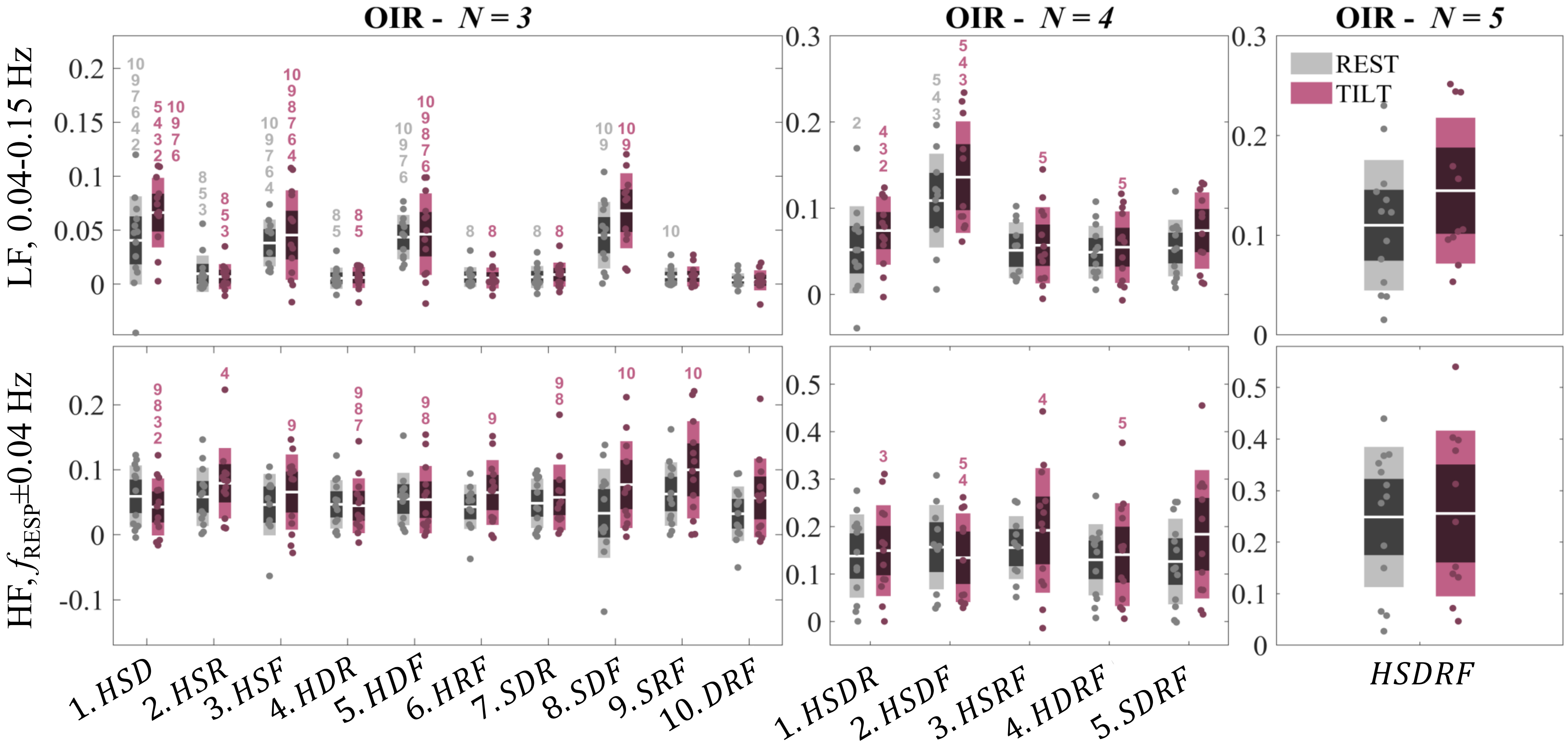


- The spectral OIR gradients peak at the respiratory frequency, revealing dominant redundancy
- Physiologically, redundancy is explained by the mechanical effects of R on S, transmitted to H via the baroreflex
- OIR values in the LF band vary significantly across conditions, with prevalent synergy at CB10 and prevalent redundancy at CB20

Application: cardiovascular, respiratory and cerebrovascular interactions

- High-order interactions at rest and during postural stress

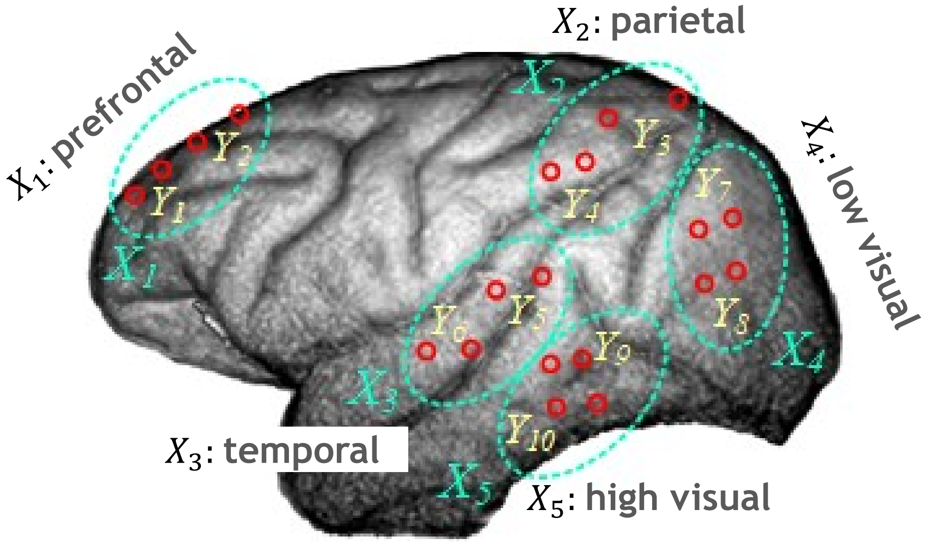




- The spectral OIR is positive in both LF and HF bands, revealing dominant redundancy
- The spectral OIR is higher in the HF band, suggesting a role of respiration in driving redundant interactions
- In the LF band, redundancy is higher for multiplets including H,S,D,F, and tends to increase with head-up tilt

Application: ECoG signals in the anesthetized macaque monkey

- Public dataset: *http://www.neurotycho.org*
- Signals from a monkey in resting awake state (REST) and during anesthesia (ANES)
- ECoG signals: 1000 Hz, downsampling 250 Hz; 160 epochs of 2 sec in each condition
- Five regions of the Default Mode Network (2 bipolar signals from each region):



- $Q = 10$ random processes $Y = \{Y_1, \dots, Y_{10}\}$ grouped in $M = 5$ blocks $X_1, \dots, X_5$

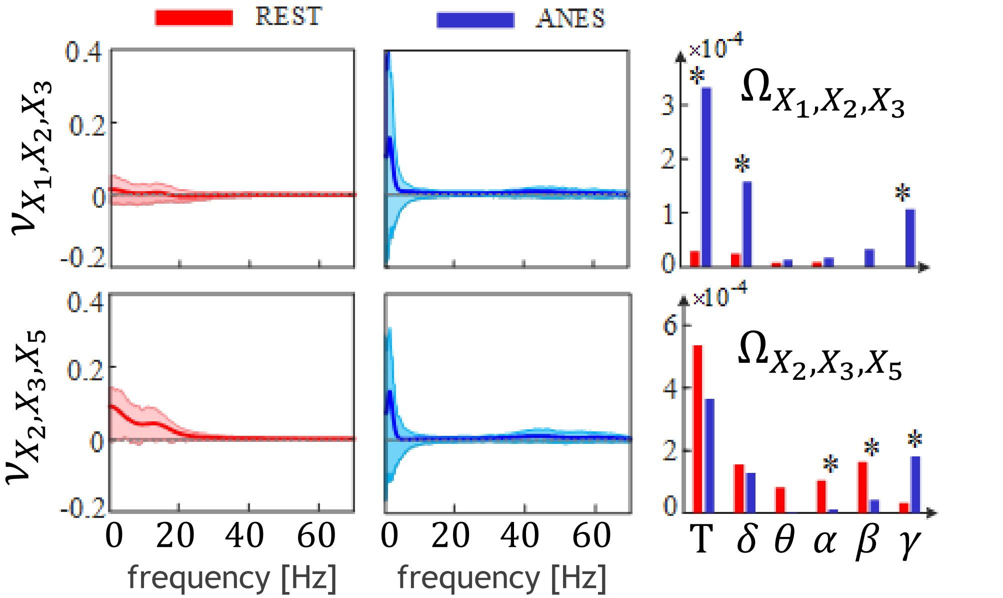
$$Y_n = \sum_{k=1}^{p} A_k Y_{n-k} + U_n$$

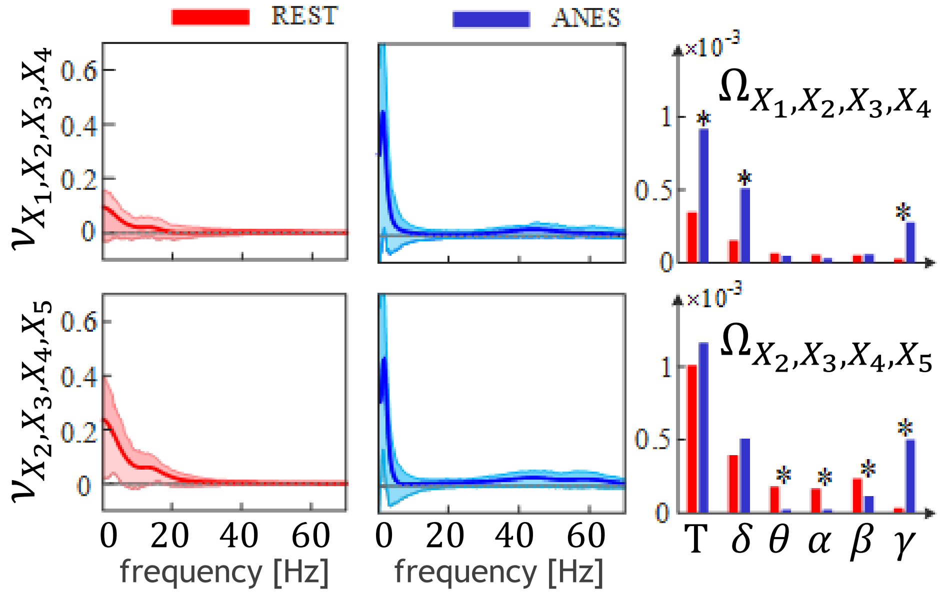
- OIR for all multiplets of order 3,4,5

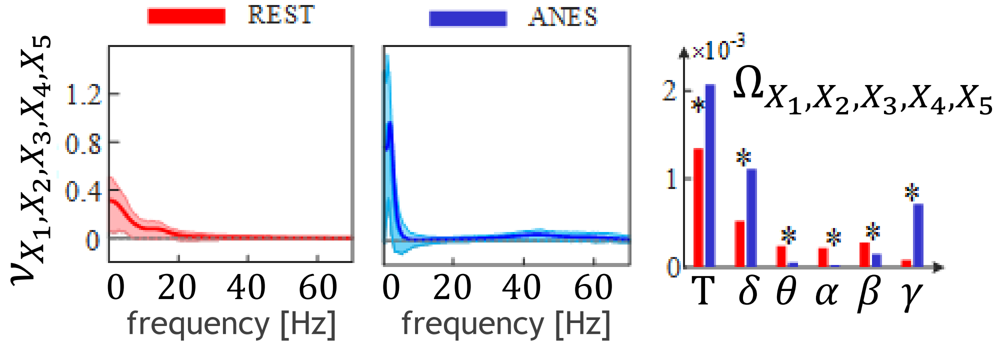
- Spectral OIR integrated in the δ (0.2-3 Hz), θ (4-7 Hz), α (8-12 Hz), β (13-30 Hz), γ (31-70 Hz) bands, and in the whole-band 0-70 Hz (time-domain OIR)

Application: ECoG signals in the anesthetized macaque monkey

- High-order interactions among brain waves during wakefulness and anesthesia





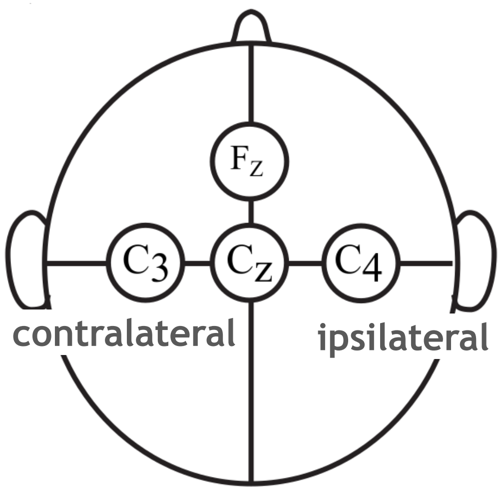


- The system is dominated by redundancy
- Multiplets involving the prefrontal cortex (X_1) display higher redundancy during ANES in δ and γ bands
- Multiplets involving the parietal, temporal and visual cortex (X_2–X_5) display lower redundancy during ANES in α and β bands

- Results support the integration theory suggesting that there is a high integration of the brain rhythms in the conscious state that disappears during the unconscious state, which is rather characterized by slow brain waves

Application: scalp EEG connectivity during motor execution

- Public dataset: *https://physionet.org/content/eegmmidb*
- Scalp EEG from 20 subjects in resting awake state (REST) and during right-fist motor execution (RIGHT)
- Sampling 160 Hz; 15 trials of 4 sec in each condition
- Four scalp regions associated with motor preparation and execution



- $M = 4$ scalar random processes

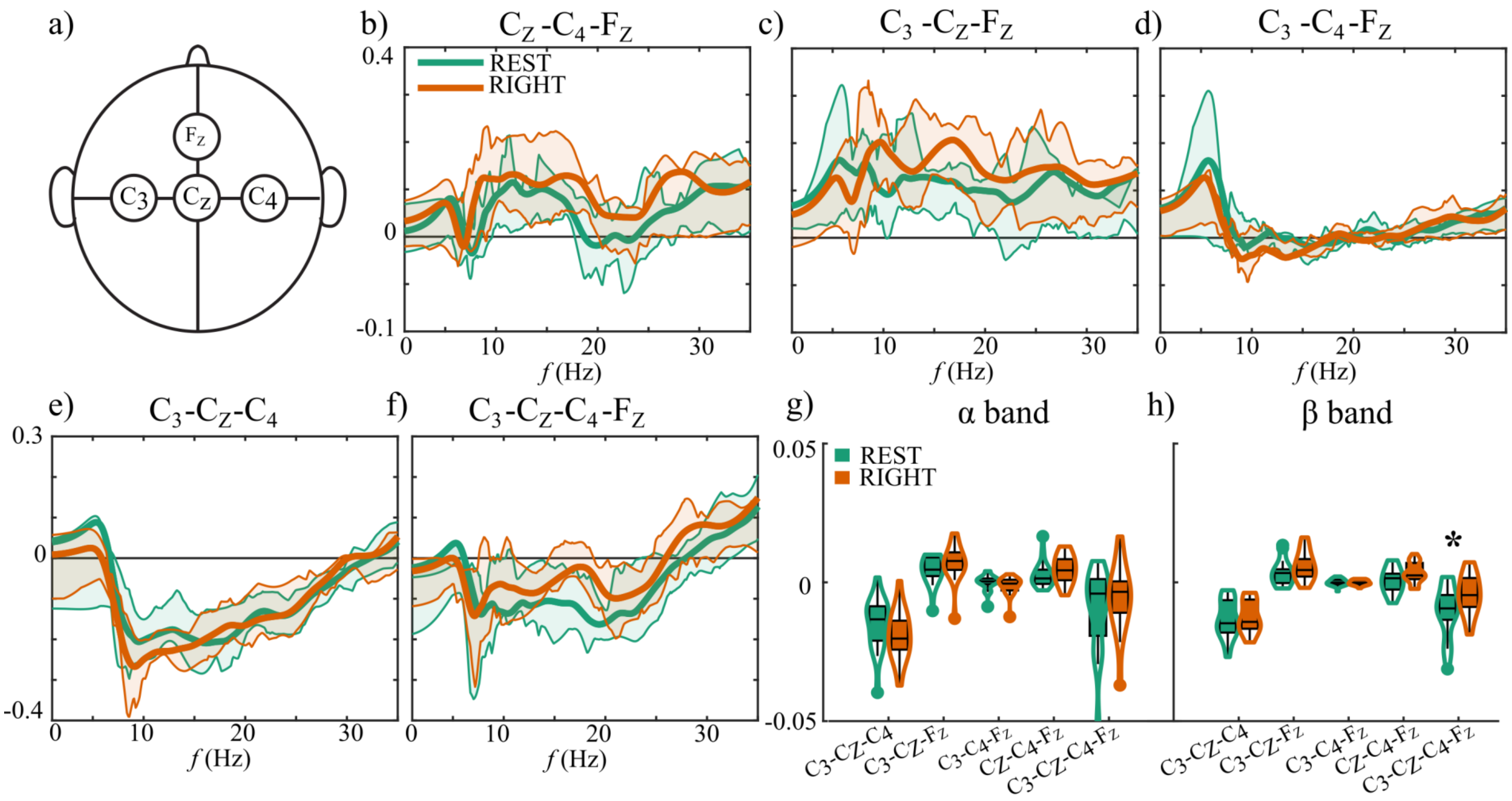
$$Y_n = \sum_{k=1}^{p} A_k Y_{n-k} + U_n$$

- OIR for all multiplets of order 3,4

- Spectral OIR integrated in the α (8-12 Hz) and β (13-30 Hz) bands involved in motor execution

Application: scalp EEG connectivity during motor execution

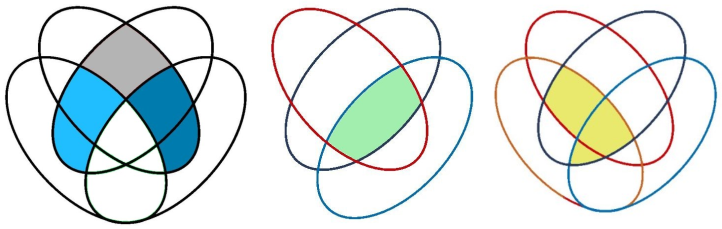
- High-order interactions among brain waves during motor execution



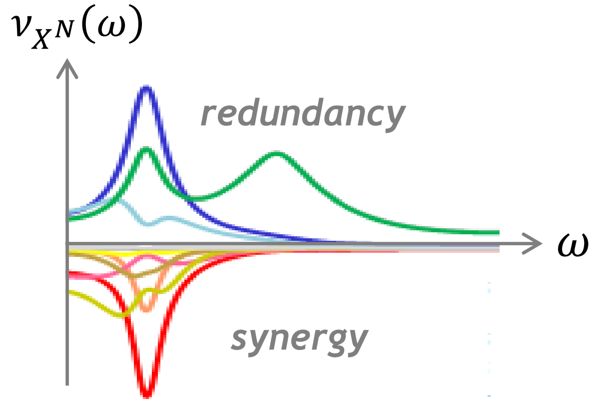
- Triplets involving two central and one lateral electrode display redundancy
- The multiplets Cz-C4-C3 and Fz-Cz-C4-C3 display synergy, reflecting ipsilateral and contralateral high-order interactions between the left and right brain hemispheres and the central regions
- Synergy is evidenced in the α and β bands linked to event-related desynchronization, and decreases during motor execution

Information Dynamics of high-order networks

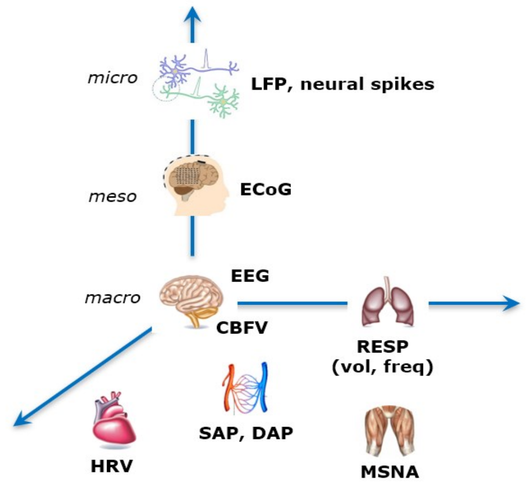
Information dynamics: developments



Spectral measures



Physiological systems



Group members: • ***Yuri Antonacci, Riccardo Pernice, Laura Sparacino, Chiara Barà***

Collaborations:

- ***Gorana Mijatovic***, *University of Novi Sad, Serbia*
- ***Sebastiano Stramaglia***, *University of Bari, Italy*
- ***Alberto Porta***, *University of Milan, Italy*
- ***Daniele Marinazzo***, *University of Ghent, Belgium*

luca.faes@unipa.it *www.lucafaes.net*